

REMARKS

Reconsideration is requested.

Claims 1-8 and 12 are pending. Claims 5-8 and 12 have been withdrawn from consideration.

Claim 1 has been revised, without prejudice, to advance prosecution. Support for the revisions may be found throughout the specification, such as on pages 12-14. No new matter has been added.

To the extent not obviated by the above amendments, the Section 112, first paragraph "enablement", rejection of claims 1-4 is traversed. Entry of the present Amendment and withdrawal of the rejection are requested in view of the above and the following further comments.

Clarification of the Examiner's reliance on and/or reference to McCarthy (Nature Reviews Cancer, Vol 5, 2005, page 839) (see page4 of the Office Action dated January 5, 2010) is requested in the event the rejection is maintained.

The Examiner appears to appreciate that presently claimed invention does not involve the use of a PRAME inhibitor alone to treat cancer. The presently claimed invention is based on the discovery that the use of a PRAME inhibitor will allow HDAC inhibitors to be used more effectively in the treatment of a tumour.

At the time of the present invention it was known that HDACs are involved in the control of cell proliferation and differentiation such that aberrant HDAC activity plays a

role in cancer. Thus, HDAC inhibitors were investigated and found to be useful in the treatment of cancer (paragraph bridging pages 3 and 4 of the application).

The presently claimed invention recites known HDAC inhibitors, in an effort to advance prosecution. The present inventors knew from the art that PRAME is over-expressed in a variety of human malignancies (page 4, lines 15-24) but, at the time of the present invention, no function had been attributed to PRAME.

The present inventors discovered that PRAME is able to confer resistance to HDACi (pages 28-29) and that PRAME expression confers cellular resistance to retinoic acid (RA) in tumours (pages 34-35). Accordingly, the presently claimed invention results from the discovery that, by inhibiting PRAME expression (using a PRAME inhibitor), the known activity of an HDACi or retinoid to treat a tumour could be put to more effective use.

The claims recite the tumours in which PRAME was known at the time of filing of this application to be over-expressed. The application as filed describes that inhibition of the expression of PRAME using an interfering RNA in a melanoma allows an HDACi to be used more effectively to treat that melanoma where previously the PRAME conferred resistance to the HDACi (page 33).

The application teaches one of ordinary skill in the art how to make and use the claimed invention without undue experimentation. One of ordinary skill in the art will appreciate from the specification that the inhibition of expression of PRAME using an interfering RNA in any of the recited cancers, i.e. cancers known to be typified by an

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over-expression of PRAME, would allow more effective treatment of that cancer by an HDAC inhibitor or retinoid.

Withdrawal of the Section 112, first paragraph, rejection is requested.

The claims are submitted to be in condition for allowance and a Notice to that effect is requested. The Examiner is requested to contact the undersigned, preferably by telephone, in the event anything further is required.

Respectfully submitted,

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